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(54) Title: MATERIALS AND METHODS RELATING TO INHIBITING THE INTERACTION OF p53 AND mdm2

(57) Abstract

Mdm2 binds to p53 in cells in which mdm2 is not overexpressed, i.e. in cells in which mdm2 is expressed at normal or low levels, and that in these cells, this interaction targets the p53 for degradation. This finding means that inhibiting mdm2 production and/or inhibiting the binding of mdm2 to p53 allows levels of p53 to increase by reducing the clearance of p53 by mdm2, and can be used to activate p53 function in cells other than those in which mdm2 is overexpressed. This allows the use of an agent having the property of disrupting the binding of p53 and mdm2 or inhibiting the production of mdm2 in a population of cells, in the preparation of a medicament for activating p53, wherein the population of cells do not overexpress mdm2. Such medicaments are useful in the treatment of conditions such as cancer, viral infections or conditions in which p53 or mdm2 is not functional.



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INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/GB 98/01144

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K38/17 C12N5/10 G01N33/50 C07K16/18

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 20238 A (UNIV JOHNS HOPKINS) 14 October 1993 cited in the application see page 7, paragraph 5 see page 10, paragraph 3 - page 12, paragraph 1 ---- WO 96 02642 A (UNIV DUNDEE ;PICKSLEY STEVEN MICHAEL (GB); LANE DAVID PHILIP (GB)) 1 February 1996 cited in the application see page 1, paragraph 1 see page 3, paragraph 2 - page 6, paragraph 2 ---- -/-	1-11
X		1-11

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
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- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- "&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 August 1998	01/09/1998
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Authorized officer Sitch, W

INTERNATIONAL SEARCH REPORT

Int Application No
PCT/GB 98/01144

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BLAYDES ET AL: "TOLERANCE OF HIGH LEVELS OF WILD-TYPE P53 IN TRANSFORMED EPITHELIAL CELLS DEPENDENT ON AUTO-REGULATION BY MDM-2" ONCOGENE, vol. 14, no. 15, 17 April 1997, pages 1859-1868, XP002075048 cited in the application see page 1859 see abstract see page 1866, paragraph 3 ---	1-11
X	BÖTTGER ET AL: "IDENTIFICATION OF NOVEL MDM2 BINDING PEPTIDES BY PHAGE DISPLAY" ONCOGENE, vol. 13, 1996, pages 2141-2147, XP002075049 cited in the application see the whole document	1-11
A	DATABASE MEDLINE FILE SERVER STN KARLSRUHE ABSTRACT 93390942, KOVAR ET AL: "NARROW SPECTRUM OF INFREQUENT P53 MUTATIONS AND ABSENCE OF MDM2 AMPLIFICATION IN EWING TUMOURS" XP002075050 see abstract & ONCOGENE, vol. 8, no. 10, October 1993, pages 2683-2690,	---
P, X	WO 98 01467 A (CIBA GEIGY AG ;CANCER RES CAMPAIGN TECH (GB); LANE DAVID (GB); BOE) 15 January 1998 see the whole document see page 11, paragraph 4 - paragraph 5 see page 16, paragraph 2 - page 17, paragraph 1 -----	1-28

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 98/01144

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:

because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 12-21 partially, insofar as they concern in vivo methods, are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. Claims Nos.:

because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l Application No

PCT/GB 98/01144

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